EXHIBIT B

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CONTROL NO.	FILING DATE	PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
95/000,074	01/31/2005	6680306	

EXAMINER
Leigh Maier

ART UNIT	PAPER
1623	

FISH & NEAVE IP GROUP
ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

DATE MAILED:

10/18/05

INTER PARTES REEXAMINATION COMMUNICATION

BELOW/ATTACHED YOU WILL FIND A COMMUNICATION FROM THE UNITED STATES PATENT AND TRADEMARK OFFICE OFFICIAL(S) IN CHARGE OF THE PRESENT REEXAMINATION PROCEEDING.

All correspondence relating to this *inter partes* reexamination proceeding should be directed to the **Central Reexamination Unit** at the mail, FAX, or hand-carry addresses given at the end of this communication.

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(THIRD PARTY REQUESTER'S CORRESPONDENCE ADDRESS)

STEPHEN J. GAUDET, PH.D.
PERKINS SMITH & COHEN LLP
ONE BEACON STREET 30TH FLOOR
BOSTON, MA 02108

Transmittal of Communication to Third Party Requester
Inter Partes Reexamination

REEXAMINATION CONTROL NUMBER *95/000,074*.

PATENT NUMBER *6,680,306*.

TECHNOLOGY CENTER *1600*.

ART UNIT *1623*.

Enclosed is a copy of the latest communication from the United States Patent and Trademark Office in the above-identified reexamination proceeding. 37 CFR 1.903.

Prior to the filing of a Notice of Appeal, each time the patent owner responds to this communication, the third party requester of the *inter partes* reexamination may once file written comments within a period of 30 days from the date of service of the patent owner's response. This 30-day time period is statutory (35 U.S.C. 314(b)(2)), and, as such, it cannot be extended. See also 37 CFR 1.947.

If an *ex parte* reexamination has been merged with the *inter partes* reexamination, no responsive submission by any *ex parte* third party requester is permitted.

All correspondence relating to this inter partes reexamination proceeding should be directed to the **Central Reexamination Unit** at the mail, FAX, or hand-carry addresses given at the end of the communication enclosed with this transmittal.

OFFICE ACTION IN INTER PARTES REEXAMINATION	Control No.	Patent Under Reexamination	
	95/000,074	6680306	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address. --

Responsive to the communication(s) filed by:
Patent Owner on 13 June 2005
Third Party(ies) on 15 July 2005

RESPONSE TIMES ARE SET TO EXPIRE AS FOLLOWS:

For Patent Owner's Response:
2 MONTH(S) from the mailing date of this action. 37 CFR 1.945. EXTENSIONS OF TIME ARE GOVERNED BY 37 CFR 1.956.
For Third Party Requester's Comments on the Patent Owner Response:
30 DAYS from the date of service of any patent owner's response. 37 CFR 1.947. NO EXTENSIONS OF TIME ARE PERMITTED. 35 U.S.C. 314(b)(2).

All correspondence relating to this inter partes reexamination proceeding should be directed to the **Central Reexamination Unit** at the mail, FAX, or hand-carry addresses given at the end of this Office action.

This action is not an Action Closing Prosecution under 37 CFR 1.949, nor is it a Right of Appeal Notice under 37 CFR 1.953.

PART I. THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892
2. ☐ Information Disclosure Citation, PTO-1449 or PTO/SB/08
3. ☐ _____

PART II. SUMMARY OF ACTION:

1a. ☒ Claims 1-44 are subject to reexamination.
1b. ☐ Claims _____ are not subject to reexamination.
2. ☒ Claims 5,6,12 and 13 have been canceled.
3. ☐ Claims _____ are confirmed. [Unamended patent claims]
4. ☐ Claims _____ are patentable. [Amended or new claims]
5. ☒ Claims 1-4,7-11 and 14-44 are rejected.
6. ☐ Claims _____ are objected to.
7. ☐ The drawings filed on _____ ☐ are acceptable ☐ are not acceptable.
8. ☐ The drawing correction request filed on _____ is: ☐ approved. ☐ disapproved.
9. ☐ Acknowledgment is made of the claim for priority under 35 U.S.C. 119 (a)-(d). The certified copy has: ☐ been received. ☐ not been received. ☐ been filed in Application/Control No _____.
10. ☐ Other _____

DETAILED ACTION

Status of the Claims

Claims 1, 2, 4, and 9 have been amended. Claims 5, 6, 12, and 13 have been canceled. Claims 24-44 are newly added. Claims 1-4, 7-11, and 14-44 are pending. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections Proposed by Third Party Requester

Ground #1. The Requester submitted that claim 1 is unpatentable under 35 USC 102(e) as being anticipated by Klyosov et al (US 6,645,946), as set forth in the previous Office action. Requester further submitted that claims 3, 4, and 17-21 are unpatentable under 35 USC 102(e) as being anticipated by, or in the alternative, unpatentable under 35 USC 103(a) as being obvious over Klyosov et al (US 6,645,946), also as set forth in the previous Office action.

The rejection of claims 1, 3, 4, 17, and 20, under 35 U.S.C. 102(e) as being anticipated by Klyosov et al (US 6,645,946) proposed by the requester was adopted in the first Office action. However, in view of the amendments to the claims this rejection is not adopted. The amendment regarding inhibiting the growth of a tumor presupposes a tumor in the patient that is treated. The mice treated in the reference are healthy.

The rejection of claims 1, 3, 4, and 17-21 under 35 U.S.C. 103(a) as being obvious over Klyosov et al (US 6,645,946) proposed by the requester, is adopted. This rejection is maintained, as discussed below.

Claims 1, 3, 4, and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klyosov et al (US 6,645,946).

Klyosov '946 teaches as set forth in the previous Office action. The claims have been amended to require a patient in need of treatment. The preamble is further amended to indicate that the intent of the method is to inhibit growth of a tumor.

The reference teaches as set forth previously. The reference is silent regarding inhibition of tumor growth.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer galactomannan with an oncolytic chemotherapeutic in order to reduce side effects produced by the chemotherapeutic agent with a reasonable expectation of success. As noted above, the reference is silent regarding inhibition of tumor growth. However, the same patient population would be treated, and recognition of another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. In the absence of unexpected results, it would be within the scope of the artisan to determine the optimum mode of administration and protocol regarding the relative timing of administration of the components through routine experimentation.

In the response filed June 13, 2005, the patent owner submits a declaration under 37 CFR 1.131 from Yan Chang ("Chang declaration"). This declaration purports to demonstrate that the presently claimed subject matter was conceived and reduced to practice prior to the earliest priority date of Klyosov '946. The Chang declaration tabulates data from a study designed to test

the efficacy of IFN-α2b, GBC590B, and combinations thereof, in a pancreatic carcinoma xenograft mouse model. The Chang declaration concludes that these data demonstrate that GBC590B enhances the efficacy of interferon-α2b (IFN-α2b). This conclusion is based on the fact that the combination treatment results in the survival of some animals, while admitting that the mean day of survival (MDS) did not improve.

The declaration is defective because a declaration by less than all named inventors of an application is accepted where it is shown that less than all named inventors of an application invented the subject matter of the claims under rejection. However, in this case, declarant states "I am *a co-inventor* of the abovementioned patent ..." (Emphasis added) See MPEP 715.04 [R2]. It is noted that correction of inventorship may also be made during reexamination. See 37 CFR 1.324 and MPEP § 1481 for petition for correction of inventorship in a patent. If a petition filed under 37 CFR 1.324 is granted, a Certificate of Correction indicating the change of inventorship will not be issued, because the reexamination certificate that will ultimately issue will contain the appropriate change-of-inventorship information (i.e., the Certificate of Correction is in effect merged with the reexamination certificate)

In the response filed July 15, 2005, the requester has submitted declarations disputing Dr. Chang's inventorship. The declarations submitted by Drs. Platt and Nir allege that in March 1999, Dr. Platt had conceived of using modified pectin (GBC-590, apparently the same or similar product as GBC590B, discussed above) in combination with IFN for the treatment of cancer. A copy of a contemporaneous fax, dated 3/11/99, (sent by Dr. Platt and received by Dr. Nir) discussing this idea appears to be consistent with, but not proof of, this allegation. It is also consistent with Dr. Sasak's account that Dr. Platt conceived of the idea.

All three of these declarations (Platt, Nir, and Sasak) contend that Dr. Chang was not involved in the conception of using modified pectin in combination with IFN. This allegation is noted. However, declarants submit no additional evidence to support this.

The examiner further notes that 37 CFR 1.131 calls for original records or photocopies thereof to support the claimed date of invention, while the exhibit submitted appears to be table excerpted from the Piedmont Research Center report, submitted by the Requester. This report is a final compilation of data apparently from a series of experiments that may or may not have been signed and witnessed. Although the date(s) could be redacted, original documents would be expected to be dated. Declarant does not provide an explanation for the absence of said records or photocopies. These omissions are also noted by the requester.

The examiner further notes that there is insufficient explanation of the data presented in the Chang Declaration. (One must look to the Piedmont Research Center report, submitted by the Requester, for that. This submission is addressed below.) It is not clear how there can be "survivors" in some test groups while, as declarant admits, there is no improvement in the MDS.

It is further noted that the claims have been amended wherein "enhanced efficacy" is manifested in inhibition of tumor growth. The Chang declaration does not address tumor inhibition, per se. That is, there is no observation of tumor size. Neither is there any exhibit demonstrating conception, much less reduction to practice, of a galectin-binding agent to enhance surgical treatment.

The Requester further notes in comments filed July 15, 2005 that GBC590 is used in combination with IFN and contends that IFN is a biologic agent and not a chemotherapeutic. To support this contention, declarations from Drs. Aguilar-Cordova, Zabrecky, and Zetter have been

submitted. These declarations have been reviewed and are found to be convincing. The examiner further notes that the terms "interferon" (or "biologics") and "chemotherapy" are used in the alternative in the art, much like "gene therapy" and "chemotherapy." See below.

The Requester has submitted the report generated by Piedmont Research Center ("report"), from which the data in the Chang Declaration appear to be taken. This report includes analysis of the data derived from the treatment of mice with GBC560B in combination with IFN. The report includes an analysis of the data with the conclusion that the combination of agents does not demonstrate efficacy and that any long term responders are "likely because of biological variation in the response of tumor-bearing mice to an agent that produces a variable level of efficacy." See page 6 of the report.

The requester further notes that the data submitted in the Chang declaration was not cited to the Office pursuant to 37 CFR 1.56. This observation is noted; however, the examiner finds no particular requirement for its submission during prosecution.

In view of the foregoing, it is the opinion of the examiner that the Chang declaration fails to demonstrate conception of the invention before the priority date of Klyosov '946.

Ground #2. The requester submitted that claim 1 is unpatentable under 35 USC 102(e) as being anticipated by Klyosov et al (US 2003/0064957), as set forth in the previous Office action. Requester further submits that claims 3, 4, and 17-21 are unpatentable under 35 USC 102(e) as being anticipated, or in the alternative, unpatentable under 35 USC 103(a) by Klyosov et al (US 2003/0064957), also as set forth in the previous Office action.

The rejection of claims 1, 3, 4, and 17-21 under 35 USC 102(e)/103(a) based on Klyosov '957 as proposed by the requester is adopted. The rejections are maintained, as discussed below.

Claims 1, 3, 4, 17, and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Klyosov et al (US 2003/0064957).

Klyosov '957 discloses the administration of galactomannan and 5-FU by injection to mice having induced tumors. See example 3. The combination results in a synergistic effect on tumor reduction. The reference also describes the structure of galactomannan. See paragraph [0042]. This structure appears to meet the criteria of carbohydrates that would bind to galectin-1 or galectin-3.

Claims 1, 3, 4, and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klyosov et al (US 2003/0064957).

Klyosov '957 teaches as set forth above. The reference does not exemplify oral administration or sequential delivery of the galactomannan and oncolytic agent. However, the reference further suggests a variety of modes of administration, including oral, and sequential administration of the galactomannan and chemotherapeutic agent. See paragraphs [0032] and [0048].

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer galactomannan with an oncolytic chemotherapeutic in order to increase the efficacy of the chemotherapeutic in the treatment of cancer with a reasonable expectation of success. The artisan would be motivated to administer this combination because

the art had taught that galactomannan reduces the side effects of toxic chemotherapeutic agents. As discussed above, the reference discloses a clear enhancement of efficacy in synergistic tumor reduction. In the absence of unexpected results, it would be within the scope of the artisan to determine the optimum mode of administration and protocol regarding the relative timing of administration of the components through routine experimentation.

In response filed June 13, 2005, the patent owner cites the Chang declaration, discussed above. This declaration purports to demonstrate that the presently claimed subject matter was conceived and reduced to practice prior to the earliest priority date of Klyosov '957. This declaration fails to demonstrate conception of the invention before the priority date of the reference, for reasons set forth above. In the response filed July 15, 2005, the requester has no further remarks regarding this ground of rejection. The rejections are maintained as repeated above.

Ground #3. The requester submitted that claim 1 is unpatentable under 35 USC 102(e) as being anticipated by Klyosov et al (US 6,642,205). Requester further submits that claims 3, 4, 17 and 18 are also anticipated, or in the alternative, unpatentable under 35 USC 103(a) as being obvious over this reference.

The proposed rejection is not adopted for the reasons set forth in the first Office action, and the examiner's position remains unchanged. The patent owner acknowledges this with no further comment.

The Requester contends in comments filed July 15, 2005 that the definition of "concomitant" in claim 1 brings within the scope of the claim a covalent linkage between the

carbohydrate and chemotherapeutic. The examiner respectfully disagrees. The examiner maintains that the claim construction contemplates the agents being such that they may be administered concomitantly *or* separately. In any case, the amendment requiring a polymeric carbohydrate makes the argument moot.

Grounds #4 and 5.

Ground #4. The Requester submitted that claims 1 and 2 are unpatentable under 35 USC 102(b) as being anticipated by Rubin et al (US 5,639,737). The requester further submits that claims 3, 17, 18, 20, and 23 are unpatentable under 35 USC 102(b) as being anticipated by, or in the alternative, unpatentable under 35 USC 103(a) as being obvious over Rubin et al (US 5,639,737).

Ground #5. Requester further submitted that claim 22 is unpatentable under 35 USC 103(a) as being obvious over Rubin et al (US 5,639,737) in view of Fujimoto et al (Eur. J. Cancer, 1991).

The examiner notes that Rubin does not exemplify administration of the recited components as amended and thus does not clearly anticipate the claims. Therefore, the rejection of claims 1 and 2 under 35 USC 102(b) as proposed by the requester is not adopted.

The rejection of claims 1-3, 13, 17, 18, 20, and 23 under 35 USC 103(a) over Rubin et al (US 5,639,737) as proposed by the requester was adopted in the first Office action. However, in view of amendments to the claims, it is not adopted. Rubin teaches as set forth in the previous Office action. The reference does not teach or fairly suggest the use of a polymeric carbohydrate agent. The patent owner makes essentially the same observation.

With respect to claim 22, the examiner found, in the first Office action, that in the proposed combination of Rubin and Fujimoto, Fujimoto was superfluous, because there is no motivation to combine the references. Rubin suggests the administration of a carbohydrate having anti-metastasis activity. The carbohydrate used in Fujimoto is identified as an antitumor immunomodulator, with no anti-metastasis activity disclosed. With respect to the amended claims, this carbohydrate, sizofiran, is polymeric, but there is no suggestion that this entity binds galectin. The examiner maintains that there is no motivation to combine these references. Therefore, the rejection based on this *combination* is not adopted, and the examiner maintains this position.

Also in the first Office action, the examiner had proposed and applied a rejection of claim 22 under 35 USC 103(a) as being obvious over Rubin alone. However, in view of the amendments to the claims, this rejection is withdrawn. Rubin teaches as set forth in the previous Office action. The reference does not teach or fairly suggest the use of a polymeric carbohydrate agent. The patent owner makes essentially the same observation in remarks filed June 13, 2005.

From the first section of the requester's arguments filed July 15, 2005, it appears to be the opinion of the requester that the claims, as amended, (1) include new matter; (2) are indefinite; and (3) lack of enablement. Issues (1) and (2) are addressed further below. See "Rejections Newly Raised by the Examiner." Regarding issue (3), throughout this action, the requester has suggested anticipation and obviousness rejections that have been adopted by the examiner. An invention cannot be both anticipated/obvious *and* not enabled.

The requester cites the examiner's mention of U. S. patent application SN 08/819,356 in Ground #12 of the previous action and appears to suggest its combination with Rubin. This

application was cited in a quotation from Platt et al (US 6,500,807) wherein this patent notes that a pectin product was disclosed in SN 08/819,356. However, Platt '807 does not ascribe any anti-cancer activity to the pectin product. Platt '807, including its teaching of the pectin product which is *identified* in Platt '807 by reference to SN 08/819,356, was relied upon to reject the claims. The application, per se, was never relied upon in the rejection of the claims. Moreover, the application, per se, has not yet become a patent. Neither has it become available as a printed pre-grant publication. Therefore, it is unavailable as art to combine with Rubin.

Grounds #6-10.

Ground #6. The requester submitted that claims 1 and 2 are unpatentable under 35 USC 102(b) as being anticipated by Glinsky et al, Cancer Res. 1996. Requester further submitted that claims 3 and 21 are unpatentable under 35 USC 102(b) as being anticipated by, or in the alternative, unpatentable under 35 USC 103(a) as being obvious over Glinsky et al, Cancer Res., 1996.

Ground #7. The requester submitted that claim 1 is unpatentable under 35 USC 102(b) as being anticipated by Glinsky et al, Cancer and Metastasis Reviews, 1998. Requester further submitted that claim 3 is also anticipated by, or in the alternative, unpatentable under 35 USC 103(a) as being obvious over Glinsky et al, Cancer and Metastasis Reviews, 1998.

Ground #8. The requester submitted that claim 1 is unpatentable under 35 USC 102(b) as being anticipated by Green et al, Anti-Cancer Drug Design, 1999. Requester further submits that claim 3 is also anticipated by, or in the alternative, unpatentable under 35 USC 103(a) as being obvious over Green et al, Anti-Cancer Drug Design, 1999.

Ground #9. The requester submitted that claims 1 and 2 are unpatentable under 35 USC 102(b) as being anticipated by Glinsky et al, Clin. Exp. Metastasis, 1996. Requster further submits that claims 3 and 13 are unpatentable under 35 USC 102(b) as being anticipated by, or in the alternative, unpatentable under 35 USC 103(a) as being obvious over Glinsky et al, Clin. Exp. Metastasis, 1996.

Ground #10. The requester submitted that claim 1 is unpatentable under 35 USC 102(b) as being anticipated by Frankel et al, Proc. Am. Assoc. Cancer Res., 1997. Requester further submits that claim 13 is also anticipated, or in the alternative, unpatentable under 35 USC 103(a) as being obvious over Frankel et al, Proc. Am. Assoc. Cancer Res., 1997.

In each of Grounds #6-10, the rejections of claims under 35 USC 102(b) as proposed by the requester are not adopted, and the position of the examiner is unchanged.

In each of Grounds #6-10, the rejections of the claims under 35 USC 103(a) as proposed by the requester were adopted in the first Office action. However, in view of amendments to the claims, they are not adopted. None of the references cited teach or fairly suggest the use of a polymeric carbohydrate agent. The patent owner makes essentially the same observation in the remarks filed June 13, 2005.

The requester's arguments filed July 15, 2005 with respect to grounds #6-10 are the same as those addressed above in grounds #4-5.

Ground #11: The requester submitted that claim 1 is unpatentable under 35 USC 102(f) as being anticipated by Pro-Pharmaceuticals' Confidential Private Placement Memorandum, August 23, 2000, which the Requester contends was communicated to the Patentee.

Claims in an *inter partes* reexamination proceeding will be examined on the basis of patents or *printed publications*. A reference is proven to be a "printed publication" upon a satisfactory showing that such document has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art, exercising reasonable diligence, can locate it. It would appear that a company's confidential memo would not qualify as a printed publication and is not relevant to *inter partes* reexamination proceedings. Therefore, the rejection of claim 1 under 35 USC 102(f) as proposed by the requester is not adopted, and this position has not changed.

In remarks filed July 15, 2005, the requester contends "an argument could be made that [the Memorandum] became public once it was sent, in error, to GLGS. Therefore, the Memorandum should be considered for the purposes of this reexamination." The definition of a public document does not change depending on the type of proceeding in which it is cited. A reference will, in all proceedings, constitute a "printed publication" as long as a presumption is raised that the portion of the public concerned with the art would know of the invention even if accessibility is restricted to only this part of the public. In this case, accessibility was restricted to only a very small sub-set of this portion of the public.

Grounds #12-14:

Ground #12. The requester submitted that claims 1, 3, 4, 7, 8, 11 and 14-16 are unpatentable under 35 U.S.C. 103(a) as being obvious over Platt et al (US 6,500,807) in view of Platt et al. (JCNI, 1992).

Ground #13. The requester submitted that claim 9 is unpatentable under 35 USC 103(a) as being obvious over Platt et al (US 6,500,807) in view of Platt et al (JCNI, 1992) as applied to claims 1, 3, 4, 7, 8, 11 and 14-16 above, and further in view of Ros et al (Carbohyd. Res., 1996).

Ground #14. The requester submitted that claim 10 is unpatentable under 35 U.S.C. 103(a) as being unpatentable over Platt et al (US 6,500,807) in view of Platt et al. (JCNI, 1992) as applied to claims 1, 3, 4, 7, 8, 11 and 14-16 above and further in view of Renard et al (Carbohyd. Res., 1995).

The above-listed rejections of claims 1, 3, 4, 7-11 and 14-16 were proposed by the requester and applied by the examiner in the first action, but in view of arguments presented, these rejections are not adopted.

The patent owner, in his response filed June 13, 2005, contends that gene therapy and chemotherapy are considered as distinct treatment modalities and has submitted declarations from Drs. Zetter and Kasahara in addition to several exhibits to support this argument. The submissions have been reviewed and are found to be convincing. The examiner notes that the terms "gene therapy" and "chemotherapy" are used in the alternative in the art, much like "interferon" and "chemotherapy." See above.

The requester recapitulates and agrees with the original rejection but does not present any additional arguments for maintaining it.

Ground #15. The requester submitted that claims 2 and 17 are unpatentable under 35 U.S.C. 103(a) as being obvious over Fujimoto et al, (Eur. J. Cancer, 1991) in view of Raz et al., (Cancer and Metastasis Rev., 1987).

This rejection of claims 2 and 17 was proposed by the requester and applied by the examiner in the first action, but in view of the amendment, the rejection is not adopted.

In remarks filed June 13, 2005, the patent owner contends that the combination of references does not teach the use of a polymeric carbohydrate. The examiner agrees with this position. The patent owner submits further arguments regarding motivation or expectation of success. However, the amendment and the first argument makes these arguments moot.

The requester's arguments filed July 15, 2005, again suggest that the amended claims include new matter. This argument was addressed above.

The requester states that in order to accommodate the "polymeric" limitation, one could "combine these references with any number of references teaching modified citrus pectin ... such as, JNCI ('92) paper by Platt, U.S. Pat. No. '794 & '442 to Raz et al., and other references cited herein."

Regarding Platt, the product disclosed in this reference is nonbranched. See page 440, last sentence in the first full paragraph. Combining Platt with Fujimoto and Raz still would not lead one of ordinary skill to the invention as amended. This rejection is not adopted.

Raz et al (US 5,895,784) neither teaches nor suggests a branched product. The reference teaches a non-branched pectin product. See col 9, lines 31-35 and col 12, lines 49-53. Combining Platt with Fujimoto and Raz '784 still would not lead one of ordinary skill to the invention as amended. This rejection is not adopted.

Raz et al (US 5,834,442) neither teaches nor suggests a branched product. The reference teaches a non-branched pectin product. See col 9, lines 22-26 and col 12, lines 38-42. Combining Platt with Fujimoto and Raz '784 still would not lead one of ordinary skill to the invention as amended. This rejection is not adopted.

Regarding "other references *herein*," the examiner does not understand if the requester is referring to references cited in Platt and Raz patents or references of record in the instant reexamination proceeding. This proposed rejection combining references that are not specifically cited is not adopted.

Rejections Raised Previously by the Examiner

Claims 1, 3, 4, 7, 8, 11, 14-16, 18, and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Platt et al, US Patent 6,500,807 ('807).

This rejection of claims 1, 3, 4, 6-11, and 14-16 was proposed and applied by the examiner in the first action, has been withdrawn.

The patent owner contends that gene therapy and chemotherapy are considered as distinct treatment modalities. This argument is supported by submissions discussed above and found to be convincing.

The requester recapitulates and agrees with the original rejection but does not present any additional argument for maintaining it.

Claims 1-4, 7, 8, 11, and 14-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rubin et al (US 5,639,737) in view of Platt et al (WO 97/34907). This rejection is also applied to new claims 24-29 and 32-44.

Rubin teaches as set forth in the previous Office action. The reference does not teach the administration of modified citrus pectin, in combination with oncolytic chemotherapeutics or surgery.

Platt teaches that modified citrus pectin that has therapeutic utility in the treatment and prevention of metastatic cancer. See abstract and pp 5-6. The modified citrus pectin is a demethoxylated polygalacturonic acid which is interrupted by rhamnose residues and having branches terminating in galactose or arabinose. See Fig. 1.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to substitute any known anti-metastatic agent for lactose in the method disclosed by Rubin. One having ordinary skill would reasonably expect success in substituting the disclosed MCP because Platt had taught that MCP has this therapeutic utility. In the absence of unexpected results it would be within the scope of the practitioner to optimize the treatment protocol with respect to the timing and mode of administration through routine experimentation.

The claims have been amended as set forth above. New claims 24 and 25 recite essentially the same method as in claims 1 and 2, respectively, but the required carbohydrate is a substantially demethoxylated polygalacturonic acid which is interrupted with rhamnose residues, as required by the amended claims.

In the response filed June 13, 2005, the patent owner argues that the cited references do not teach that a carbohydrate that binds galectins and having the recited polymeric structure

would be effective at anything other than inhibiting metastasis and do not suggest that modified pectin would act to inhibit tumor growth. The examiner agrees; however, the references would make it obvious to take the steps required by the method regardless of what was or was not known about the mechanism of the modified pectin. Based on the teachings of the references, one of ordinary skill would be motivated to use the modified citrus pectin in combination with a chemotherapeutic agent or cancer surgery for reasons set forth above. The population in need of tumor inhibition would clearly have substantial, if not complete, overlap with the population in need of metastasis inhibition. The recognition of another advantage which would flow naturally from following the suggestion in the prior art cannot be the basis for patentability when the differences would otherwise be obvious.

The requester, in remarks filed July 15, 2005, agrees with the rejection and further cites other references disclosing biological activity of modified citrus pectin.

Claims 1-4, 7, 8, 11, and 14-23 are unpatentable under 35 USC 103(a) as being obvious over Fujimoto et al, (Eur. J. Cancer, 1991) in view of Platt et al (WO 97/34907). This rejection is also applied to new claims 24-29 and 32-44.

Fujimoto teaches the adjuvant administration of an antitumor polysaccharide to patients undergoing surgery for gastric cancer. The reference also suggests the addition of antitumor drugs to this protocol. See abstract. The reference further states that metastasis at the time of surgery is responsible for the recurrence of cancer. See first paragraph. The reference does not teach the administration of a galectin-binding carbohydrate, such as modified citrus pectin, in combination with cancer surgery.

Platt teaches as set forth above.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to add MCP (with or without other chemotherapeutics) to the surgical protocol of Fujimoto for the expected additive effects disclosed in the art. Fujimoto states that surgical metastases are responsible for recurrences in these patients. Therefore the artisan would be motivated to add MCP for its anti-metastatic activity with a reasonable expectation of success. In the absence of unexpected results it would be within the scope of the practitioner to optimize the treatment protocol with respect to the timing and mode of administration through routine experimentation.

The patent owner argues in the response filed June 13, 2005 that sizofiran was disclosed as an immunotherapeutic, and there would be no motivation to substitute a modified pectin for this carbohydrate. Again, the examiner agrees, but that is not what was stated in the rejection. The rejection states that it would be obvious to add the modified pectin to the Fujimoto protocol as an anti-metastatic agent, in *addition* to, not substituting for, another agent.

The patent owner further argues that the references, including Platt '807 "ascribes no independent biological activity whatsoever to modified pectin, and discusses only its use as a delivery vehicle for nucleic acids." First of all, this is not the reference used in the rejection. Furthermore, it is not typically the case that every single thing that is known about a product, such as modified citrus pectin, is specifically disclosed in every reference using said product. The fact that the patent owner can cite a reference wherein no independent biological activity is disclosed is not persuasive. The one used by the examiner does, in fact, disclose biological activity. The patent owner further contends that yet another reference (Platt, JNCI) not used in

the rejection does not suggest the ability of modified citrus pectin would impact tumor growth. The fact that this is not specifically disclosed is not relevant, as discussed above.

The requester agrees with the rejection and further cites other references disclosing biological activity of modified citrus pectin.

Claim 9 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rubin (US 5,639,737) in view of Platt et al (WO 97/34907) as applied to claims 1-4, 7, 8, 11, 14-29 and 32-44 above and further in view of Ros et al, (Carbohyd. Res., 1996).

The claims have been amended as set forth above.

Rubin teaches as set forth in the previous Office action.

Platt teaches as set forth in the previous Office action. The reference does not teach modified citrus pectin that is prepared enzymatically. However, the reference suggests that other procedures and experimental conditions may be used to prepare the MCP. See paragraph bridging pp 6-7.

Ros teaches the enzymatic hydrolysis of pectin. See pp 272-3.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use any method, such as enzymatic, known in the art to depolymerize pectin to arrive at the MCP having anti-metastatic activity for use in the method made obvious by the combination of Rubin and Platt, as set forth above. Platt had taught the general physical requirements and suggested the use of other methods. Therefore it would be within the scope of the artisan to use the method taught by Ros to prepare an appropriate product through routine experimentation with a reasonable expectation of success.

Claim10 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rubin (US 5,639,737) in view of Platt et al (WO 97/34907) as applied to claims 1-4, 7, 8, 11, 14-29 and 32-44 above and further in view of Renard et al, (Carbohyd. Res., 1995).

The claims have been amended as set forth above.

Rubin teaches as set forth in the previous Office action.

Platt teaches as set forth in the previous Office action. The reference does not teach modified citrus pectin that is prepared thermally. However, the reference suggests that other procedures and experimental conditions may be used to prepare the MCP. See paragraph bridging pp 6-7.

Renard teaches the thermal hydrolysis of pectin. See pp 156-7, section 2.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use any method known in the art, such as thermal, to depolymerize pectin to arrive at the MCP having anti-metastatic activity for use in the method made obvious by the combination of Rubin and Platt, as set forth above. Platt had taught the general physical requirements and suggested the use of other methods. Therefore it would be within the scope of the artisan to use the method taught by Renard to prepare an appropriate product through routine experimentation with a reasonable expectation of success.

Rejections Newly Raised by the Examiner

Claims 2-4, 7-11, 14-18, 22, 23, 25-37, 41, 42, and 44 are rejected under 35 U.S.C. 314(a) as enlarging the scope of the claims of the patent being reexamined. 35 U.S.C. 314(a) states that "no proposed amended or new claim enlarging the scope of the claims of the patent

shall be permitted" in an *inter partes* reexamination proceeding. A claim presented in a reexamination "enlarges the scope" of the patent claims where the claim is broader than the claims of the patent. A claim is broadened if it is broader in any one respect, even though it may be narrower in other respects.

Claim 2 has been amended: "A method for enhancing the efficacy of a surgical treatment by inhibiting tumor growth at the site of the surgical treatment [for cancer] in a patient ..." Now, the patient is not required to have cancer, as many tumors are known to be benign. Therefore this amendment clearly broadens the claim with respect to the patient population. New claim 25 is essentially the same method as claim 2 but with a more specifically recited therapeutic agent.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 7-11, 14-23, and 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the patent owner, at the time the application was filed, had possession of the claimed invention.

The requester alluded to the inclusion of new matter. However, whether the requester wished to formally raise this ground of rejection is unclear. The examiner raises it here.

Claims 1 and 2 have been amended so that the required carbohydrate "comprises a polymeric backbone having side chains dependent therefrom." The patent owner states that the

claims have been amended to incorporate a feature of claim 4. However, this amendment is an incomplete incorporation of the limitation of claim 4, and as such, does not appear to have adequate support. While the specification discusses the use of polymeric materials, it does not contemplate ones comprising any type of side chain, but only those terminated by a galactose or arabinose unit. See col 2, lines 40-43.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 7-11, 14, 15, 17-34, and 36-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The requester alluded to indefiniteness in the amended claims. However, whether the requester wished to formally raise this ground of rejection is unclear. The examiner raises it here.

Claims 1 and 2 have been amended so that the required carbohydrate "comprises a *polymeric* backbone having side chains dependent therefrom." (Emphasis added.) It is the opinion of the examiner that one of ordinary skill would construe a "carbohydrate having a polymeric backbone" as one with at least eight to ten monosaccharides, not to mention the additional side chains. This would presume a minimum molecular weight of *at the very least* 2000 daltons or so. However, dependent claims such as 14 and 15, which must be considered to be range-narrowing, allow for a minimum molecular weight of 1000 daltons. The examiner does not find any particular definition of "polymeric" in the specification that would allow for a "polymeric" entity having a molecular weight this low. These limitations appear to be in conflict

and thereby render the claims vague and indefinite. Newly added claims 24 and 25 are similarly indefinite because they require a *poly*galacturonic acid product but appear to contemplate products having a molecular weight of 1000 daltons (or less).

Conclusion

In order to ensure full consideration of any amendments, affidavits or declarations, or other documents as evidence of patentability, such documents must be submitted in response to this Office action. Submissions after the next Office action, which is intended to be an action closing prosecution (ACP), will be governed by the requirements of 37 CFR 1.116, which will be strictly enforced.

All correspondence relating to this *inter partes* reexamination proceeding should be directed:

By Mail to: Mail Stop *Inter Partes* Reexam
Central Reexamination Unit
United States Patent & Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

By FAX to: (571) 273-9900
Central Reexamination Unit

By hand: Customer Service Window
Attn: Central Reexamination Unit
Randolph Building, Lobby Level
401 Dulany Street
Alexandria VA 22314

Any inquiry concerning this communication or earlier communications from the examiner, or as to the status of this proceeding, should be directed to the Central Reexamination Unit at telephone number (571) 272-7705.

Leigh C. Maier

Leigh Maier
Primary Examiner
October 13, 2005

WILLIAM R. DIXON, JR.
SPECIAL PROGRAM EXAMINER